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Antimicrobial resistance trends in blood culture positive *Salmonella* Paratyphi A isolates from Pondicherry, India, 2005 - 2009

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Background: In the developing countries, enteric fever remains a significant problem of morbidity and mortality. *S.* Paratyphi A is the second most common cause of enteric fever after *S.* Typhi. The incidence of enteric fever caused by *S.* Paratyphi A has been increasing in South-East Asia, South Africa and the Indian subcontinent. Recently, there has been an upsurge in the occurrence of bacterial isolates that are resistant to ciprofloxacin, and the emergence of broad spectrum β- lactamases in typhoidal salmonellae constitutes a new challenge to the clinician.

Methods: Blood cultures were done for a total of 3,745 patients presenting with fever. Isolates were investigated using serotyping and antimicrobial susceptibility testing; as well as phenotypic testing for the presence of efflux pumps. Molecular analysis of quinolone resistance was investigated via the detection of mutations in the *gyrA*, *gyrB*, *parC*, and *parE* genes; restriction fragment length polymorphisms in the *gyrA* PCR fragment; and PCR screening for *qnr* gene and *aac(6')-Ib-cr* gene. Detection of β-lactamase gene by PCR-sequencing and IEF experiments. Genotypic characterization of representative *S.* Paratyphi A isolates was performed using pulsed field gel electrophoresis (PFGE).

Results: Of 284 *S.* Paratyphi A isolates obtained, 5 (1.7%) were MDR; 281 (98.9%) were NAR. Eighteen (6.3%) isolates were resistant to ciprofloxacin. All the isolates were found to be susceptible to ceftriaxone. All ciprofloxacin-resistant isolates (isolates with MIC upto 8 μg/mL) showed 3 mutations, two mutations within the QRDR of *gyrA*, and a single mutation in *parC*. Interestingly, isolates with ciprofloxacin MICs of ≥12 μg/mL had 4 mutations, two mutations within the QRDR of *gyrA*, and two mutations also in *parC*. All isolates were negative for *qnr* (*qnrA, qnrB, and qnrS*) and *aac(6')-Ib-cr* genes. There was genotypic diversity among the *S.* Paratyphi A in our region. Overall, 11 different (non-clonal) PFGE patterns were observed at 95%.

Conclusion: A high rate of ciprofloxacin resistance was observed, with steadily increasing NAR, but decreasing MDR. The fluoroquinolone use continues to expand and DCS and fluoroquinolone resistance drives the use of third-generation cephalosporin and other agents for the management of enteric fever.

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Extended-spectrum beta-lactamase and metallo-beta-lactamase-producing bacterial strains among the patients attending a tertiary care center in Nepal

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Background: The emergence of extended-spectrum-beta-lactamase (ESBL) and metallo-beta-lactamase (MBL) producing bacterial isolates has resulted in fewer therapeutic options in treatment modalities. However, no studies regarding MBLs had been done so far in Nepal and a few researches on ESBLs were also pilot studies. Therefore, this study was carried out to assess the current status of ESBL- and MBL-producing bacteria among patients attending Tribhuvan University Teaching Hospital (TUTH), Nepal.

Methods: This was a cross-sectional study conducted at Bacteriology laboratory of TUTH. A total of 1120 sputum, endotracheal secretion and bronchial washing specimens from patients suspected of lower respiratory tract infection (LRTI) were processed according to the standard methodology. Double disk synergy test (DDST) and Combination disk (CD) methods were used for the detection of ESBL- and MBL-producing isolates.

Results: Respiratory pathogens were recovered from 44.4% cases. *Haemophilus influenzae* (112, 21.0%) was the predominant isolate followed by *Klebsiella pneumoniae*, Pseudomonads, *Acinetobacter calcoaceticus baumannii* complex, *Streptococcus pneumoniae*, *Escherichia coli* and others. Multidrug resistance (MDR) was found in 53.6% of the total bacterial isolates. Twenty-four percent of the *Enterobacteriaceae* and nonfermentative isolates were ESBL-producers, majority of which included *K. pneumoniae* (43, 42.2%), Pseudomonads (8, 8.8%), *E. coli* (13, 41.9%) and *Acinetobacter* spp. For ESBL-producers, the most effective drug was found to be carbapenems, followed by cefoperazone-sulbactam and amikacin. MBL was present in 1.34% of the total gram-negative isolates (3 isolates each of *P. aeruginosa* and *Acinetobacter* spp). All ESBL- and MBL-producers were MDR. Forty-two percent of *S. aureus* were resistant to methicillin. Besides, one vancomycin resistant *S. aureus* (VRSA) was also encountered.

Conclusion: A high level of antibiotic resistance in LRTI pathogens was exacerbated by the association of ESBL and MBL. Though carbapenems were effective for ESBL-producers, the emergence of MBL-producing bacteria has resulted in confounding scene in antibiotic armamentarium. This is the first report of MBL-producing isolates from Nepal. The data can be taken as the baseline level of MBL in our set-up. The regular surveillance of resistant clones is important in developing countries like Nepal so that effective measures could be undertaken to reduce the emergence and dissemination of such strains.

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